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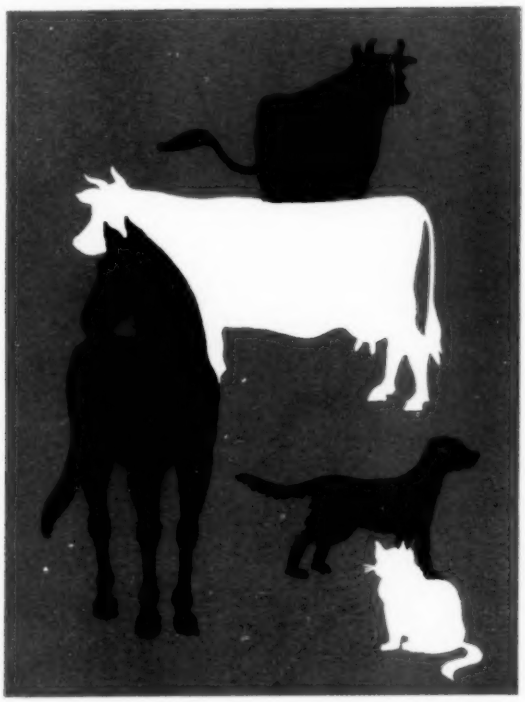

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Clinical Observations on the Use of Trimeprazine Tartrate as a Sedative and Premedicant in Horses, Cattle, Pigs and Dogs

BY

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SUMMARY.—Observations have been made on a series of 125 unselected clinical cases in which trimeprazine tartrate was used as a sedative and premedicant agent. The series includes 36 horses, 14 cattle, 10 pigs, 1 sheep and 64 dogs. The writer is of the opinion that this drug serves a useful purpose in veterinary surgery and discusses its indications and uses.

Introduction

TRIMEPRAZINE tartrate is a phenothiazine derivative with a central sedative effect which pharmacologically is intermediate between that of promethazine and chlorpromazine. It has, to an even greater degree the anti-histamine action of promethazine, and at the same time the central actions of chlorpromazine. It is largely devoid of the latter's anti-adrenaline action.

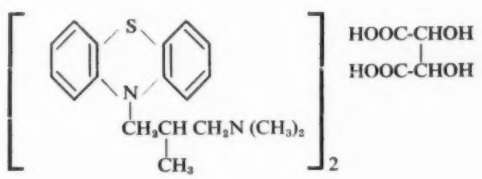
These pharmacological properties of trimeprazine have led to its use by the writer as a premedicant agent in animals prior to general anaesthesia and as a sedative agent in fractious animals.

The only communication on this subject is a short one by Mackay (1960) who noted that the premedicating properties were satisfactory when the drug was given intramuscularly in the horse.

The writer's observations have been made on 125 patients, comprising 36 horses, 14 cattle, 10 pigs, 1 sheep and 64 dogs.

Physical and Chemical Properties of Trimeprazine Tartrate

According to the manufacturers, trimeprazine is DL-10-(3-dimethylamino-2-methylpropyl) phenothiazine neutral tartrate and has the following structural formula:—



It is a white, almost odourless, non hygroscopic powder and is very sensitive to light, which causes discoloration. It is very soluble in water (1 g. in 4 c.c., at 20° C.), in methanol and in chloroform, soluble in ethanol and in acetone, sparingly soluble in *iso* propanol and insoluble in ether and benzene. The *p*H of a 1 per cent. aqueous solution is about 6. Its melting point is given as 162° C. and its molecular weight as 747.

For use in this clinical trial the drug has been presented in the form of a sterile solution in ampoules of 5 ml. Two strengths of solution have been used: a 1 per cent. w/v. solution in which each ml. contains 10 mg. and a 5 per cent. w/v solution in which each ml. contains 50 mg. The lower strength solution has been used mainly for small animals and the stronger solution for large animals.

Toxicity. The toxic symptoms are very similar to those observed following chlorpromazine administration. Intravenous injection results in a loss of muscle tone and with high doses of either compound, death is due to respiratory failure.

TABLE I
OPERATIVE AND ANAESTHETIC PROCEDURES—HORSES

Operative procedures	Ponies and riding horses	Hunters	Thoroughbreds	Shire	Donkey	General anaesthesia	Local anaesthesia	No anaesthesia	Total
Castration	1	–	–	–	1	–	2	–	2
Cryptorchidectomy	2	1	1	–	–	4	–	–	4
Examination	–	2	–	–	–	1	–	1	2
Hoof section	–	–	–	1	–	1	–	–	1
Hyo-vertebrotomy	–	–	3	–	–	1	1	1	3
Mandibular sinus investigation	2	–	–	–	–	1	–	1	2
Neoplasia	1	2	–	–	–	–	3	–	3
Nerve block	2	1	–	–	–	–	3	–	3
Neurectomy	2	–	–	–	–	2	–	–	2
Orthopaedic	–	3	–	–	–	2	1	–	3
Skin grafting	–	1	–	–	–	1	–	–	1
Transportation	1	–	–	–	–	–	–	1	1
Trephining of frontal and maxillary sinuses	–	1	–	–	–	–	1	–	1
Wamberg's operation	1	–	–	–	–	1	–	–	1
Whitehouse's operation	–	–	1	–	–	1	–	–	1
X-ray	4	1	1	–	–	–	–	6	6
Totals	16	12	6	1	1	15	11	10	36

Cases under Review

In 119 animals trimeprazine tartrate was administered intravenously and in 6 cases intramuscularly. In no instance was any reaction observed at the site of injection. The series of cases will be considered under species headings.

Horses

Trimeprazine tartrate was administered intravenously to 35 horses varying in age from 5 months to 24 years, and in weight from 2¼ to 13 cwt. The type of horse, procedures involved and methods of anaesthesia are set out in Table I.

In general the dose rate employed was 0.5 mg. per lb., although on two occasions 1.0 mg. per lb. produced no adverse effect. Signs of sedation were observed within 5 minutes of administration. The horse tended to hang its head and appeared sleepy but in most cases could be aroused by noise or handling. This state persisted for an average period of 1 hour after which the effect gradually diminished.

Indications for Use.

As a sedative. The drug may be used for the loading of recalcitrant and nervous horses for transport and for calming nervous animals during transport.

Radiographs of horses that would otherwise not stand still can be obtained with greater precision and with a definite saving of time and film.

For minor interferences, nerve blocks, etc. in the standing position the benefits are of limited value since, as previously mentioned, continued handling tends to provoke some reaction. However, it has been noticed that in recumbency the horse, whilst susceptible to stimuli, quickly returns to a state of quiet and apparent sleep. With release of the hobbles the animal readily rises and can be walked back to its box with safety.

As a premedicant. Trimeprazine tartrate facilitates protracted intravenous injections in fidgety or uncooperative patients, as for example chloral hydrate

TABLE II
ANAESTHETIC REQUIREMENTS AND RECOVERY TIMES—HORSES

Type of horse	Weight (cwt.)	Amount of chloral hydrate required (grammes)	Total recumbency time (hours)
Hunter	9½	90 + 10 gr. pentobarbitone	3½
Shire	13	90	9
Pony	7½	45	1
Hunter	9	90	3½
Riding horse	8½	90	1½
Pony	5¼	82	2
Pony	4½	30	1½
Thoroughbred	3¾	55	2½
Riding horse	8	60	1¾
Hunter	12	60	1
Thoroughbred	9	75	2½
Hunter	9½	90	6

administration in the standing position. The horse stands more quietly and goes down gently. Eight horses have been cast by the intravenous administration of succinylcholine chloride following sedation with trimeprazine tartrate. These animals have gone down easily and have remained quiet after application of hobbles. They respond normally to stimulation after the effect of the relaxant drug has worn off, normally within 6 minutes of injection.

Trimeprazine tartrate has preceded general anaesthesia in 15 animals. The anaesthetic agents were intravenous chloral hydrate in 12, thiopentone sodium in 1, and thiopentone sodium followed by halothane/oxygen in 2.

There was no indication that premedication with trimeprazine tartrate reduced the amount of either barbiturate or chloral hydrate required. There was, however, a noticeable prolongation of the recovery time following chloral hydrate anaesthesia. In 2 cases the increase was very marked, being 6 hours and 9 hours respectively. The requirements of chloral hydrate and the recovery times are shown in Table II. In all cases, recovery was calm and uneventful.

One horse was given trimeprazine tartrate intramuscularly. It was a nervous animal and a

TABLE III
OPERATIVE AND ANAESTHETIC PROCEDURES—CATTLE

Operative procedure	Bulls	Steers	Cows	Heifers	Calves	General anaesthesia	Narcosis and local anaesthesia	Local anaesthesia	No anaesthesia	Total
Closure of rumenal fistula	–	–	–	1	–	–	–	1	–	1
Examination	2	–	–	–	–	–	–	–	2	2
Experimental surgery ...	–	1	–	2	3	6	–	–	–	6
Foot trimming	–	–	1	–	–	–	–	–	1	1
Neoplasia	1	–	–	1	–	–	–	2	–	2
Urethrotomy	1	–	–	–	–	–	1	–	–	1
X-ray	–	–	–	–	1	–	–	–	1	1
Total	4	1	1	4	4	6	1	3	4	14

notoriously bad traveller. It was given 0.7 mg. per lb. 30 minutes before being loaded into its box, at which time it was quiet and co-operative. On being unloaded it showed no effects of the journey and was certainly much calmer than on previous occasions.

Cattle

Twelve animals received trimeprazine tartrate by the intravenous route and 2 intramuscularly. The weight range was from 90 lb. to 16 cwt. Ages were from 2 weeks to 5 years. The dose rate varied from 0.5 mg. per lb. to 1.3 mg. per lb. bodyweight. In most cases 1.0 mg. per lb. was employed.

When injected intravenously the sedative effect was much more marked and was noticeable within 2 to 7 minutes of completion. The animals would appear sleepy and tend to lie down, although in all cases they were able to stand if required. The sedative effect was more marked in the younger animals and this was distinctly advantageous if clipping and shaving were necessary.

The type of animal and the operative and anaesthetic procedures are shown in Table III. In the 6 cases requiring general anaesthesia, induction was by intravenous thiopentone sodium and maintenance was by cyclopropane/oxygen in 5 and by halothane/oxygen in 1. All these animals received routine premedication with atropine sulphate. The trimeprazine tartrate had little or no influence on the amount of thiopentone required. Recovery on all occasions was quiet.

The indications for the use of this drug in the bovine animal are as a routine premedicant prior to general anaesthesia and as a sedative in unruly animals. A typical example of its sedative effect was in a 2-year-old Red Poll heifer weighing 5¼ cwt. admitted for the removal of a large neoplasm. She had not previously been handled and was wild and unmanageable. Five minutes after receiving 750 mg. of trimeprazine tartrate intravenously, she was completely amenable to manipulation and infiltration of the tissues with local anaesthetic solution.

It has been used in 2 bulls, but has had no marked effect on the relaxation of the penis.

In the 2 animals in which trimeprazine tartrate was given intramuscularly at the rate of 1.0 mg. per lb., the degree of sedation was very slight.

Pigs

Seven pigs received trimeprazine tartrate intravenously and 3 intramuscularly. The 10 cases were made up of 6 Landrace, 2 Large White and 2 Saddlebacks. Their weights ranged from 20 lb. to 350 lb. and their ages from 5 weeks to 3 years. The dose rate was 1.0 mg. per lb. intravenously or 1.5 to 3.0 mg. per lb. intramuscularly.

TABLE IV
OPERATIVE AND ANAESTHETIC PROCEDURES—PIGS

Operative procedures	General anaesthesia	Local anaesthesia	No anaesthesia
Caesarean section ...	1	–	–
Repair of fractured tibia	1	–	–
Repair of scrotal hernia	1	3	
Sedation prior to ringing	–	–	3
X-ray	–	–	1

The pigs which received the drug by the intravenous route showed quite a marked degree of sedation within 5 to 10 minutes of injection. They were easily roused but for operation under local anaesthesia the sedation was effective. The operative and anaesthetic procedures are shown in Table IV.

For general anaesthesia, induction in 2 cases was by intravenous thiopentone sodium. Maintenance was by ether/oxygen in one and halothane/oxygen in the other. Induction in the third case was by intravenous pentobarbitone sodium and maintenance by halothane/oxygen. The amount of barbiturate required in each was found to be a little less than would have been expected without premedication. Induction and recovery in all cases was quiet.

In 2 of the pigs given trimeprazine tartrate intramuscularly, there was little if any appreciable sedative effect. One of these was given a dose rate of 1.5 mg. per lb. and the other 3.0 mg. per lb. The third pig was a Large White sow presented for caesarean section. This animal, however, with a dose rate of 1.5 mg. per lb. was certainly quieter within 45 minutes of injection and exhibited no marked response to stimulation.

The principle indication for the use of this drug in the pig is to quieten an animal before induction of general anaesthesia and during operations under local anaesthesia. Radiographic procedures are also facilitated.

Sheep

The only ovine case was a 7-year-old Suffolk ram of 210 lb. presented for vasectomy. It was given

TABLE V
OPERATIVE AND ANAESTHETIC PROCEDURES—DOGS

Operative procedures	Number of cases	General anaesthesia	Local anaesthesia	Thiambutene HCl	No anaesthesia	To cut down excitement after thiopentone anaesthesia
Amputation	2	2	–	–	–	–
Anal stenosis	1	1	–	–	–	–
Anal sac extirpation	2	2	–	–	–	–
Aural resection	3	3	–	–	–	–
Diaphragmatic hernia	1	1	–	–	–	–
Enterotomy	3	3	–	–	–	–
Examination	4	1	–	1	1	1
Intrathoracic	1	1	–	–	–	–
Laparotomy	2	2	–	–	–	–
Neoplasia	5	3	2	–	–	–
Ophthalmic	4	4	–	–	–	–
Orthopaedic	21	18	2	–	1	–
Ovarohysterectomy	2	2	–	–	–	–
Ovarohysterectomy-pyometritis	3	3	–	–	–	–
Pyloric stenosis	1	1	–	–	–	–
Urethrotomy	2	2	–	–	–	–
X-ray	7	–	–	–	7	–
Totals	64	49	4	1	9	1

250 mg. of trimeprazine tartrate intravenously and appeared well sedated within 10 minutes. Thirty minutes after injection, the operation site was prepared and infiltrated with local anaesthetic solution, which provoked some struggling. A further 100 mg. of trimeprazine tartrate was given intravenously after which the animal lay quietly on the operating table throughout the operation. On completion the animal could stand and walk but was still well sedated, preferring to lie down and sleep. Recovery was uneventful.

Dogs

Sixty-three dogs of 22 different breeds were given trimeprazine tartrate intravenously. They weighed from 3 to 80 lb. and their ages ranged from 9 weeks to 15 years. For operative and anaesthetic procedures see Table V.

Dosage and Toxicity

The dose rates of trimeprazine tartrate used in this series fall into 2 main groups. A dose rate of 2.0 mg. per lb. bodyweight as a sedative prior to examination, radiography or operation under local anaesthesia and a dose rate of 1.0 mg. per lb. bodyweight for premedication prior to general anaesthesia. Dose rates between these two levels have been employed in odd cases, and in one 3.0 mg. per lb. was given with safety. Dogs subjected to the higher dose rates did not lose the ability to stand but the sedative effect was more pronounced. Four dogs were given a repeat dose without ill effect. In 3 instances part of the injection went subcutaneously and produced no reaction.

A 17-year-old Border Terrier bitch (not included in the 64 dogs which were given trimeprazine tartrate therapeutically) was presented for euthanasia. It weighed 25 lb. and was given 250 mg. trimeprazine tartrate intravenously. Recumbency occurred in 30 seconds, and in 2 minutes the respirations were very shallow but the pulse was strong. Within 5 minutes the respirations had returned to normal. At this stage the corneal reflex was present but the pedal reflex absent. A further 250 mg. trimeprazine tartrate was given 10 minutes after the initial dose. Respirations ceased after 1 minute and the pulse became weak. Two minutes later gasping respirations commenced and continued for 3 minutes. The animal died from respiratory depression after a further 7 minutes. The initial dose rate used here was 10 times higher than the therapeutic dose and the final dose used to produce death was 20 times the therapeutic dose.

Sedative effects

The effect of trimeprazine tartrate is noticeable within 1 to 5 minutes of injection but the degree of sedation with a given dose rate varies somewhat from dog to dog. Sedated dogs respond to noise by raising the head or trying to get up. There was a most marked response in 5 dogs.

Clipping and shaving are more easily carried out under trimeprazine tartrate and this obviously results in a major saving of anaesthetic time. Manipulation and examination by students has also been accomplished with ease and with the minimum interference to patients. In teaching institution this must add to the value of its use.

In painful conditions there was no marked analgesic effect. Such dogs were much easier to handle, but would whine and occasionally attempt to bite. In painful fracture cases it was necessary to conduct manipulations under general anaesthesia. Postoperative pain was controlled by pethidine hydrochloride given intramuscularly at a dose rate of 1 to 2 mg. per lb.

One dog which was insufficiently sedated after a dose of 2.0 mg. per lb. trimeprazine tartrate was given 5.0 mg. per lb. diethyl thiambutene hydrochloride subcutaneously. This gave excellent relaxation and sedation for examination followed by a normal recovery.

Trimeprazine tartrate has also been given at the rate of 1.0 mg. per lb. to a dog in order to counter narcotic excitement during recovery from thiopentone sodium anaesthesia. The dog became quiet within 1 minute and subsequent recovery was smooth.

One dog received trimeprazine tartrate intramuscularly. After a dose of 3.6 mg. per lb. it only showed a slight degree of sedation. The dog was known to be vicious and was still inclined to bite when approached.

Premedicant Uses

Trimeprazine tartrate has been used in 49 dogs subjected to general anaesthesia (Table VI). Muscular relaxation was excellent in every case and bleeding at the operation site was not noticeably affected. Where gaseous anaesthetics were employed atropine sulphate was given as a routine premedicant.

TABLE VI
ANAESTHETIC TECHNIQUES—DOGS

Method of anaesthesia	Number of cases
Pentobarbitone	16
Pentobarbitone ether/oxygen	3
Thiopentone	4
Thiopentone ether/oxygen	2
Thiopentone nitrous oxide/oxygen/ether	11
Thiopentone cyclopropane/oxygen ...	8
Thiopentone halothane/oxygen ...	5

Barbiturate potentiation was noted in all but 3 cases, the computed dose being reduced by a factor of $\frac{2}{3}$ to $\frac{3}{4}$. Of the 3 exceptions, 2 dogs required the full computed dose and the other required one third more than the computed dose. Megimide sodium was administered post-operatively by slow intravenous injection in selected cases, and when it was employed no untoward effects were noticed.

Recovery from general anaesthesia was quiet in all but 4 cases in which there was whining, which undoubtedly was associated with pain. They were given pethidine hydrochloride and the whining ceased in 5 to 10 minutes. Recovery times have varied according to the anaesthetic agents used. With gaseous anaesthetics and with cyclopropane in particular the recovery times have been within the range of 15 to 45 minutes. With barbiturates alone recovery has been longer varying from 1 to $3\frac{1}{2}$ hours. In those cases where it was used alone or with local anaesthesia, most of the sedative effect wore off within 1 hour, and although the animals tended to sleep if undisturbed, they were readily able to walk.

Other Species

One patient not included in the series of 125 received trimeprazine tartrate. This was a 3-year-old male Chinese Water Deer with a fractured mandible. It was very excitable and struggled violently when handled. It weighed 28 lb. and was given 30 mg. of trimeprazine tartrate intravenously. The animal was much quieter 5 minutes later and lay still for radiography. Three grains of thiopentone intravenously gave excellent anaesthesia for 15 minutes which enabled reduction and fixation of the fracture. The animal made a quiet recovery.

Discussion

It is not possible to be dogmatic concerning the value of sedative drugs in animals, but from the experience gained in the series under review it would appear that trimeprazine tartrate can serve a useful purpose in veterinary procedures.

Administration by the intravenous route is apparently safe and the resultant sedation more marked and the onset more rapid than when given intramuscularly. Animals can be aroused from the sedated state on stimulation and there is no analgesic effect. This must be borne in mind when dealing with fractious or vicious animals. The drug is most useful to control animals during radiographic procedures and operations under local anaesthesia.

As a premedicant trimeprazine facilitates preanaesthetic preparation of the patient giving a valuable saving of anaesthetic time. Potentiation has been noted where barbiturates have been used in dogs and pigs. Induction of anaesthesia has been quiet and recovery smooth in all cases.

A variety of drugs have been given to patients following premedication with trimeprazine. None of these have shown any signs of antagonism. Trimeprazine tartrate has in fact shown itself to play a valuable part in a number of types of balanced anaesthesia.

Acknowledgments.—The author wishes to thank Professor C. Formston, Dr. G. H. Arthur, Mr. L. C. Vaughan and Miss H. Briggs of the Department of Surgery for their co-operation in this work, and Messrs. May & Baker Limited for generous supplies of the drug.

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HILL FARMING RESEARCH ORGANISATION: NEW GOVERNING BODY

The Secretary of State for Scotland, after consultation with the Ministry of Agriculture and the Agricultural Research Council, has appointed a new governing body for the Hill Farming Research Organisation, who will serve for three years as from April 1st, 1960. The new members are:—

Lord Stratheden and Campbell (chairman), chairman of the governing body of the Edinburgh and East of Scotland College of Agriculture; Professor G. F. Boddie, Professor of Veterinary Medicine and Pharmacology at Edinburgh University; Mr. J. T. Beresford, west country farmer; Mr. Peter Cameron, hill farmer; Professor W. Ellison, Professor of Agriculture (crop husbandry) at the University College of Wales; Mr. R. E. Grieve, Border hill farmer.

Professor D. S. Herdrie, Principal of the West of Scotland Agricultural College, Professor of Agriculture at Glasgow University; Professor E. L. Hirst, Professor of Organic Chemistry at Edinburgh University; Mr. Gwyn Jones, Welsh sheep farmer; Principal M. A. H. Tincker, Principal of the North of Scotland College of Agriculture; Mr. J. Vickers, farmer in County Durham; Professor S. J. Watson, Principal of the Edinburgh and East of Scotland College of Agriculture, Professor of Agriculture at Edinburgh University, member of the Agricultural Research Council; Professor P. E. Weatherley, Professor of Botany at Aberdeen University.

Immunity to Helminths—Recent Advances*

BY

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THOUGH the title would appear to limit the context of this lecture a little consideration for what might be called an alternative title—"advances in the knowledge of host-parasite relationships"—indicates that the study of immunity to parasites embraces not a narrow chauvinistic field but extends to almost all fields of biology, certainly microbiology. We are not concerned simply with the interplay of antigen and antibody, we are concerned with the interplay of a population of parasites on a population of animals and as such the picture becomes complex with almost frightening swiftness. Whitlock (1955) has expressed this complexity in an attractive manner by stating that the common equation *Bacillus anthracis* plus sheep equals disease, however the common equation *Haemonchus contortus* plus sheep equals no disease. If one wants to delineate an equation with *H. contortus* on one side and disease on the other it is necessary to add to the *H. contortus* side genetic make up of the host, lambing time, soil microclimate and several other things including nutrition. With such a statement of what might lead to disease we have some hint as to the complexity of the spectrum of factors which lead to the establishment of an immune population. Indeed if one looks at the broad subject of immunology in its modern concept it is seen that included in its tentacles are such things as blood group genetics, skin grafting, cancer, autoimmune diseases and perhaps even fertilisation. It would appear that in these modern days the world is suffering from an excess of fertilisation: we are constantly informed by politicians, economists and the like that rapidly the world is being over-populated and food shortage, even famine, may well stare us in the face in the next few decades. Apart from the increased need to grow more crops and raise more animals there is the ever pressing need to eliminate disease from the animal population of the world and here it is necessary to take the international view. No doubt other speakers will consider the bacterial and virus diseases, and though these are all parasites, my brief will be restricted to the conventional parasites, those animals living within another animal. We are still ignorant of the total effect of parasitism either in this country or in the world at large. One cannot but be impressed by the statement of account of parasitic helminth diseases in the Animal Health Year Book of F.A.O. (1958). In almost all countries of the world gastro-intestinal nematodiasis, intestinal taeniasis, fascioliasis and verminous bronchitis are recorded as being "widespread throughout the country." Some day it may be possible to estimate the loss caused; the recent work of Spedding *et al.* (1955, 1958) in this country might indicate that it is very great. Spedding has shown that what are generally considered to be normal burdens of intestinal worms are responsible for considerable reduction in live-weight gain, up to 30 per cent. in one group of ewes under study and further deleterious effects may be seen in the offspring of parasitised ewes as compared with worm-free ewes.

Not only must we look to the parasitic diseases of animals as a means of increasing the world food supply but again we must take the international view and realise that parasitic diseases of man bring ill health and early death to millions of human beings year after year with facinorous persistence. It is of some importance that these diseases, which are the direct causes of weakness and ineffectiveness of people in the potential food growing areas of the world, be reduced or eliminated. Means immunological are actively being studied in this and other countries and information garnered from both the medical and veterinary fields is of value to either.

In many diseases, bacterial and viral, efficient control measures exist, being based on eradication or vaccination. Eradication in the case of helminth diseases is generally regarded as something very difficult to achieve, nevertheless the elaborate work of Spedding (1954 1956) who raised lambs helminth free and folded them over pasture to avoid infection may not be as impracticable as it may seem, indeed where lambs are sold fat at an early age there may be advantages in it. The procedure of vaccination is still in its early stages in helminth infections, but a notable start has been made in the use of a vaccine for parasitic bronchitis and the promise of comparable vaccines for other parasitic diseases opens the door for the control of parasites on a large scale. Rather than detail the possible uses of vaccines in helminth diseases we shall concern ourselves with the reasons why animals become immune to parasites and attempt to answer the questions "what are the essential materials required by the animal from the parasite?" and "how do the immune mechanisms affect a parasite or rather a population of parasites?" One point of warning necessary here is that when one considers helminths it must be realised that several species exist which differ not only in their morphology but also in their biology and the immunity which they induce. There is every indication at present that each species is specific as far as the immunological response goes, certainly as far as generic level the immunities appear to be distinct; thus sheep resistant to *Trichostrongylus colubriformis* are susceptible to *H. contortus*, nor does previous infection with *H.*

* This paper was delivered as a Peter Wilson Bequest Lecture at the Royal (Dick) School of Veterinary Studies, Edinburgh, on February 10th, 1960.

contortus confer resistance to Trichostrongylus spp. (Stewart, 1950). It is to be hoped that this resistance is not at a species level since if this was so one could have an animal immune to *T. vitrinus* but susceptible to *T. colubriformis*. In countries where a few species are of importance this would make little difference but in other instances where parasite burdens are a mixture of several species then vaccination would have to be " polyvalent " in character.

Before going deeply into the mechanisms of resistance perhaps it is pertinent to mention the rôle played by genetic mechanisms. Perhaps for some several thousand years stock owners have recognised that some animals and some places are more beneficial to their requirements than others. Even to-day in certain areas of this country it is well known that certain breeds thrive better and perhaps in all branches of infectious disease modern science has paid more attention to cures and potions and much less to the importance of genetics in disease. Evidence of genetic resistance to disease has been abundantly clear to plant scientists for many years and has provided one of the most fruitful approaches to the control of disease in that other kingdom of life. Breed differences in the susceptibility of sheep to parasites have been recorded by Cameron (1935) and some suggestion that this might be linked to the haemoglobin and potassium blood types of sheep (see Evans, Harris & Warren, 1958) has been made by Evans (1958). Whitlock (1955) has particularly concerned himself with genetic factors in parasitism and has demonstrated a genetic base in his experiments for resistance to *H. contortus*, an effect which he has designated the *violet effect*. He would go as far as to say that there are sufficient grounds to recommend a change of rams following any outbreak of trichostrongylidosis.

The foregoing has served to indicate the complexity of the host parasite relationship. No attempt has been made to simplify it because it is not a simple relationship. This does not mean that it cannot be elucidated or that no attempt should be made to do so.

At the start of an explanation as to how the mechanisms of immunity work a satisfactory point of departure is an observation made by Stoll in 1929. Stoll infected lambs with *H. contortus* and placed them on an enclosed pasture. During the ensuing weeks the faecal egg count rose to high levels and then there was a dramatic fall in egg counts to negative values, this being associated with loss of worms. Despite subsequent frequent reinfection with large numbers of infective larvae the lambs remained refractory to reinfection. Stoll designated this " Self cure and protection " this being one of the first demonstrations of the way domestic animals respond immunologically to their parasite burdens. Stoll's results on experimental lambs are generally applicable to natural conditions. In sheep in Britain there occurs a phenomenon called the Spring Rise (see Morgan *et al.*, 1947, 1950, 1951 and 1952, and Crofton, 1954) which is characterised by a marked increase in worm egg output and this is also associated with an increased worm burden at this time. Immunological studies on this phenomenon (Soulsby, 1957a) have shown that the termination of the spring

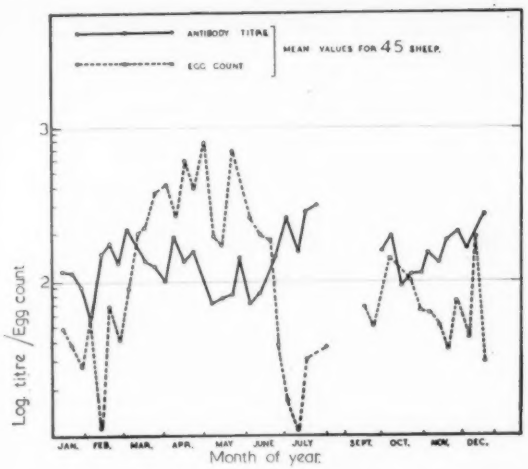

FIG. 1.—Mean antibody titre and mean number of eggs per gramme of faeces of 45 sheep throughout the year. To demonstrate the spring rise phenomenon and its termination by a flock self-cure mechanism.

rise has all the attributes of a flock self-cure mechanism, this being associated with a marked increase in the mean nematode antibody titre of the flock (see Fig. 1). Following this self-cure mechanism the mean egg output of the flock during late summer is low despite the fact that at this time pasture contamination is high (Crofton, 1949). Hence as a result of the self-cure mechanism a reasonable degree of protection has been conferred on the flock. These results are applicable to the adult members of the flock and if during the period of protection susceptible animals are introduced then they will reflect the challenge to which the adults are being subjected and are resisting. This is in fact seen in the case of lambs of the flock which show a marked rise in egg count during this period of protection of the adults (Crofton, 1955). It is a well recognised feature of parasitism that it is the young animals which suffer to the greatest degree.

During the last few years new information has accumulated about the self-cure mechanism. This mechanism is not restricted to *H. contortus* infection and it is likely that many nematode infections are terminated by some comparable reaction, one of these being *Dictyocaulus viviparus* infection (Wetzel, 1948). Stewart (1953, 1955) in Australia has studied the self-cure reaction in detail and has found that it is initiated in suitably sensitised sheep by a challenge dose of larvae. The reaction is not too specific since *H. contortus* larvae will not only induce self cure of a *H. contortus* population but also causes elimination of other abomasal parasites such as *T. axei* and *Ostertagia circumcincta* and also stimulates self cure of intestinal *Trichostrongylus* spp. Though *H. contortus* larvae will self-cure intestinal infections, *Trichostrongylus* spp. larvae, though inducing self cure of adults of that species, will not affect a *H. contortus* infection. The reason for this may be the antigenic constitution of the two species but more likely

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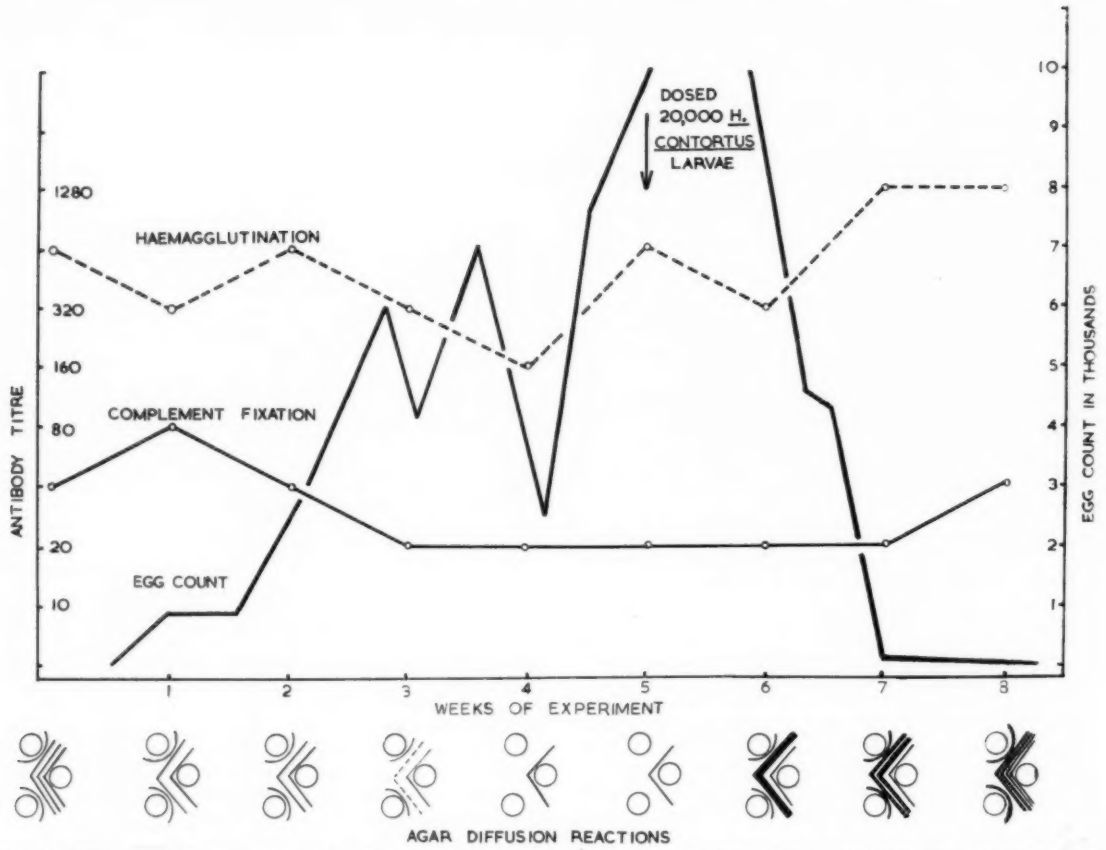

FIG. 2.—The serological response of a sheep undergoing the self-cure mechanism after a challenge dose of larvae. To demonstrate the marked response at the time of self cure and the variation in response in the course of the infection.

because antigenic material from the abomasum can pass readily to the duodenum whereas similar material can not easily pass from the duodenum to the abomasum (Stewart, 1955). The mechanism of elimination appears to be some alteration in the environment of the mucosa which makes parasitism impossible (Stewart, 1955), what these changes are is uncertain but a reduction in oxygen tension in such an area has been suggested (Soulsby, 1957b). The self-cure reaction is a local reaction at the infected area of the digestive tract and examination of the mucosa of a self cured sheep shows that there is a marked oedematous change with a superficial aggregation of eosinophils. Such a change is suggestive of a hypersensitive response and indeed Stewart (1955) was able to show that a significant rise in blood histamine occurred at the time of self cure. Suppression of the histamine by antihistamine drugs eliminated the self-cure reaction. The occurrence of this hypersensitive reaction gives a good time marker as to when exactly the reaction takes place since in almost all cases hypersensitive reactions in parasites are of the immediate type as distinct from the tuberculin type of reaction. Stewart found that the rise in histamine occurred between the second and fourth day after the administration of larvae. This has important implications in that the mere entry of infective larvae into the animal does not trigger off the self-cure reaction, but some development is necessary on the part of the larvae before materials are available which will initiate the process of self cure. Recent work in Australia (Soulsby, Sommerville & Stewart, 1959, Soulsby & Stewart, 1960) has shown that the moulting of larvae in the abomasum is most probably the mechanism for the initiation of the self-cure reaction. By infecting sheep and slaughtering them at intervals it was found that up until the third ecdysis of the challenging dose of larvae the existing adult population of *H. contortus* remained intact but when the moult of larvae from the third to the fourth larval stages occurred adult parasites were eliminated from the abomasum. Associated with the self-cure mechanism there is an antibody response which can be detected by conventional serological tests, but it occurs after self cure has taken place and is still in evidence when the self-cure reaction has been suppressed by antihistamine drugs. As such it would appear that circulating antibody plays no part in the self-cure mechanism. Nevertheless at this time the serological

response is particularly interesting since a marked reaction occurs with a substance responsible for the exsheathment or ecdysis of larvae, exsheathing fluid (Soulsby, Sommerville & Stewart, 1959). Exsheathing fluid is secreted by infective larvae from a region

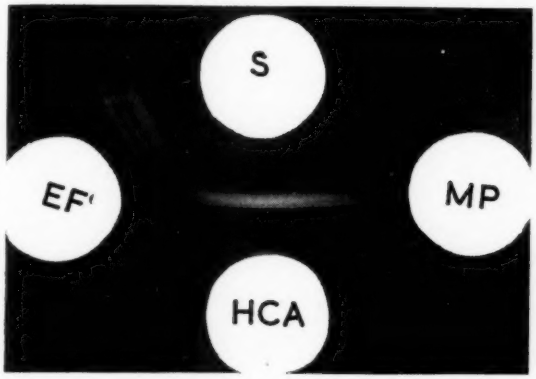

FIG. 3.—The relationship of the marked serological response at the time of self cure to exsheathing fluid.
S = Serum taken at time of self cure.
E.F. = Exsheathing fluid.
HCA = *H. contortus* antigen.
MP = Metabolic products.

near the base of the oesophagus of the larva being activated by a dialysable factor or factors in the alimentary canal of the host, this fluid acts on a circumscribed region of the cuticle which eventually fractures and allows the larva to escape (Sommerville, 1957). The normal serological reaction in resistant sheep to *H. contortus* as judged by agar diffusion precipitin tests consists of four distinct bands (Soulsby & Stewart, 1960). The variation of these during infection will be reported elsewhere but a study of these at the time of self cure illustrates not only the marked serological response at that time and its relationship to exsheathing fluid (see Figs. 2 and 3) but also the marked variation in response which can occur during a nematode infection. The moulting period of larvae is thus incriminated in being responsible for one of the phenomena of immunity to nematodes. Its importance in general in the stimulation of immunity to helminths has been recently stressed by Soulsby (1959). One point which needs emphasis is that the response to infection is an ever varied one. It must be realised that a nematode population from infection to maturity is subject to vast changes. From a relatively primitive infective larvae with no genital system and little excretory system there evolves in three weeks or less an adult worm possessing a complicated reproductive system which in the case of an adult female *H. contortus* will lay eggs at the rate of 5,000 per day (Martin & Ross, 1934). Such vast changes in behaviour, both physiological and morphological will of necessity call forth a variation in response from the host.

Let us now turn from self cure to protection. The effects of protection are diverse and may embrace virtual complete protection to reinfection, suppression of development to maturity or simply suppression of egg production in female worms. We have yet to learn whether these effects are the function of a single reaction or a limited number of reactions or whether there is a multiplicity of reactions responsible for all these effects. Are there for example specific anti-oogenesis antibodies which inhibit egg production or antibodies which inhibit the growth of genitalia, cuticula or intestinal cells, all of which are phenomena which are in evidence in developing parasites and which are depressed in an immune animal.

In recent years much stress has been laid on the importance of the so-called "metabolic products" of parasites as agents which immunise the host in an effective manner. In fact such antigens have been designated "functional" antigens (Oliver-Gonzalez, 1946b) since they are thought to induce a functional, *protective*, immunity as against merely raising antibodies which can be detected by serological tests. Support came for these metabolic products since it had been shown that when larvae of certain nematodes were immersed in immune serum precipitates developed around the various natural orifices of the larvae. Examples of this are seen in the case of hookworms (Otto, 1939) *Trichinella spiralis* (Mauss, 1940) and *Ascaris lumbricoides* (Oliver-Gonzalez, 1946a) (see Fig 4). Further support for the importance of these products is given by the fact that in general the immunity induced by non viable parasite tissues is of a low order only, whereas the living parasite induced a good degree of resistance: metabolic products are associated with the living parasite. Vaccination trials with metabolic products have had some degree of success in the case of experimental infections such as *T. spiralis* (Campbell, 1955) *Nippostrongylus muris* (Thorson, 1953) and *A. lumbricoides* (Soulsby, 1957c). The immunity induced by these metabolic products was of a lower order than induced by actual infection but difficulties exist in obtaining large amounts of metabolic products.

The author is inclined to the opinion that, though metabolic products may be of some importance, they are not the main source of "functional" antigen and that somewhere in the life cycle within the host there are more important times for the release of such antigens. Studies with *A. lumbricoides* have shown that one of the important periods for the release of such antigens is the time of the moulting period. In an immune animal, the challenge dose of infective larvae is allowed to enter the host and is even allowed to grow to a certain extent but the larval population is not allowed to develop through the moulting period and concomitantly the parasite population is rapidly killed off. Experiments using a natural marker antibody, the Forssman antibody (Soulsby, 1958), have shown that it is at this time of the moult that antigen release first can be detected in any large amount, in fact the earlier larval stages, *i.e.* those prior to the moult, contribute little to the antigen production. This is supported by the observation that such larvae are little affected by the immune mechanisms since they are allowed to grow somewhat and also such early larvae are unaffected by immune serum in any visible way as distinct from older larvae which show

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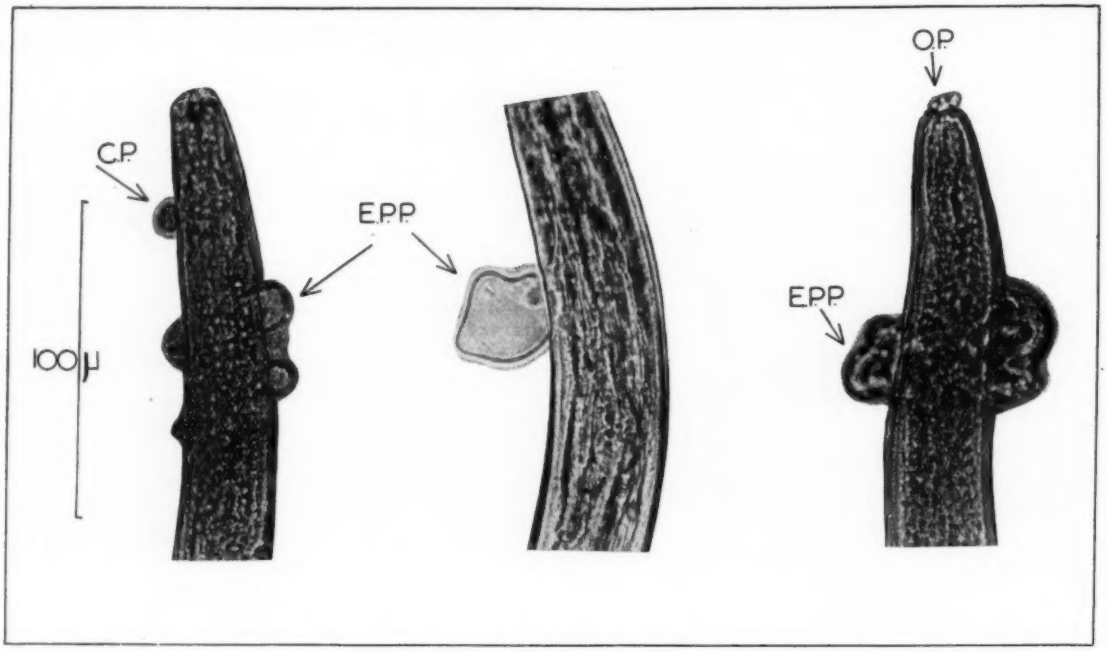

FIG. 4.—Third-stage *A. lumbricoides* larvae after immersion in immune serum.
O.P. = Oral precipitate.
E.P.P. = Excretory pore precipitate.
C.P. = Cuticular precipitate.

characteristic precipitate at various orifices. In experiments with *Trichostrongylus* spp. in immune sheep (Soulsby, 1958, unpublished) it was also found that the challenge dose of infective larvae was allowed to establish itself for a few days but was not allowed to enter the moulting phase and was also eliminated at this time. This type of reaction occurs in an animal which possesses a high degree of immunity. One can envisage that where the immunity is not of such a high order then total inhibition of moulting and elimination of the infection may not occur. In the case of experimental ascaris infection moulting is only delayed when immunity is of a low order and in the many instances where delayed development of larvae occurs it is probably due to the inhibition of the moulting period by an immune response not powerful enough to completely kill the parasite. Whatever the immune mechanism is, it must be there the whole time since removal of the inhibited larvae to non-immune animals will allow normal development (Chandler, 1936). In many cases it is fairly clear that retardation of development is the function of an immune response; Michel (1952) has described inhibition of development at a late larval stage in the case of rabbits resistant to *T. retortaeformis* infection and Stewart (1958) demonstrated a retardation of moulting in cattle resistant to *Cooperia* infection, this author also demonstrated a delay in exsheathment of the infective larvae in such animals. There are other instances however when retardation of development cannot be immediately ascribed to the conventionally understood immune mechanisms thus in some cases retarded growth appears to be dictated by the presence of adult worms and in the case of *H. placei* in cattle large numbers of larvae may remain dormant in the mucosa being somehow retarded by the presence of adult worms. When the latter are removed by anthelmintic treatment larval development is initiated and severe and even fatal infection may develop (Roberts, 1956).

In recent experiments with an X-irradiated vaccine for *H. contortus*, Jarrett *et al.* (1959) demonstrated that immunity is induced by a short period of larval development, adult stages apparently being unnecessary for the induction of resistance. They found also that if infective larvae were irradiated too much, immunity was greatly reduced. It is possible to ascribe this to a suppression of development to such an extent as to eliminate any moulting phase in the development and hence, if the postulates regarding the importance of the moulting period in immunity are valid, to eliminate the important source of protective antigen. It is known that increasing doses of irradiation increasingly affect the ability of nematodes to develop and persist in an animal (Gould *et al.*, 1957).

It would be thought that, since this moulting period appears to be of some signal importance, if it were possible to culture larvae *in vitro* then the materials liberated at the time of the moulting process should serve as efficient vaccines and as such be essentially

non-viable vaccines. Some process has been made in this field and Silverman (1960) using *in vitro* culture techniques has been able to induce satisfactory immunity with material from culture forms of larvae after they have passed through the moult leading to the fourth larval stage. The time is not far distant when parenteral vaccines prepared from parasites cultivated *in vitro* will be available as commercial preparations.

The evidence so far incriminates the moulting period as an important time when antigens which stimulate protective immunity are released. It is appreciated that this may not be the only phase of the infection which is of importance. With the increased use of *in vitro* techniques it will now be possible to investigate much more fully the importance of various larval stages as immunising agents. Until such techniques were available we had to be content with observations on the behaviour of a population of parasites and evidence which was to some extent circumstantial. Now we shall be able to observe directly the effect of the defence mechanisms on the various parasitic larval stages.

We are still in ignorance as to the essential reactions which take place within the parasite when it is attacked by the immune mechanisms. Possibly internal enzymes are inhibited; those for example which are concerned with the formation of new cuticle, oogenetic tissue and the like. Alternatively the action may be more fundamental and interfere with the mitosis of cells, the inhibition of some essential growth substance or even inhibition of the synthesis of nucleic acid. Only further research work will delineate these mechanisms. But at last we have working hypotheses of the immune reactions to helminths, firstly that this is dependent essentially on the living parasite and secondly that there are certain phases of the parasitic life cycle which are important. With these bases in mind it is now possible to understand part of the mechanism and to plan an attack based on these tenets.

Having dealt in detail with some of the mechanisms of immunity to parasites we will now glance briefly at the broader implications of immunity and immunisation. This can be drawn up as a credit and debit balance to some extent. On the credit side we have the means to prevent frank disease as is instanced by the use of an X-irradiated larval vaccine for Dictyocaulus infection in calves. Some promise is given for a similar type of vaccine for the stomach parasite *H. contortus* both in cattle (Ross *et al.*, 1959) and sheep (Jarrett *et al.*, 1959) and vaccines prepared from cultivated forms may soon be past the development stage. The possession of a polyvalent or multispecies vaccine would make it possible to eliminate the spring rise in the helminth population of sheep since this is due to a lowering of the immune status of the flock during the winter (Soulsby, 1957a), similarly lambs may well be protected at weaning time against the ravages of intestinal parasites later in the year.

On the debit side immunity presents a more complicated picture but mainly resolves itself into the depression of development whilst yet allowing a parasite population to persist, mention has already been made of the behaviour of *H. placei* in cattle. The behaviour of Ostertagia spp. in various species is the subject of much research and clinical disease has been ascribed to heavy larval populations (Martin *et al.*, 1957). It is not unlikely that such a phenomenon is due to an immune mechanism and the use of vaccination procedures may accentuate such an eventuality and lead to " occult " helminthiasis being a condition to be reckoned with yet difficult to diagnose and treat. Perhaps the greatest danger in the use of helminth vaccines is the tendency to imagine that a vaccine against one parasite will protect against all. There is still the unfortunate tendency to regard all intestinal parasites as just " worms " and such an attitude of mind may lead to the relaxation of husbandry with unfortunate results. However it is difficult to see how these disadvantages could even outweigh the advantages of creating a protective immunity. The creation of a resistance to parasites in young animals comparable to that in adults can bring nothing but good to the food animals of this country in particular and those of the world in general.

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Clinical Note

Fractured Skull in the Bovine Animal

A. G. Southerton and J. R. B. Dawson

Warwick

WE have recently encountered two interesting cases of compressed fracture of the skull in cattle.

Case 1

Subject. A 3-month-old Friesian heifer.

History. The calf had eaten normally on the evening prior to our first visit, but the following morning refused food, was excitable and had a staggering gait.

Examination. There were no external injuries and palpation of the skull revealed no abnormality. The calf had a vacant expression with haphazard response to stimuli of light, touch and noise. The gait was staggering, there was grinding of the teeth and kicking at the abdomen. Temperature was normal.

Diagnosis. Encephalitis. The possibility of phenol poisoning was considered as the pens had been treated recently.

Prognosis. An unfavourable prognosis was given.

Treatment. It was decided to give symptomatic treatment for a few days.

Progress. The calf took gruel quite well but the nervous symptoms became progressively worse over the course of the next 4 days, the calf having increasing difficulty in standing and finally becoming prostrate with marked nystagmus. It was decided to slaughter the animal.

Post-mortem Examination. Post-mortem examination of the head showed a compressed fracture of the frontal bone on the left side with extensive haemorrhage over the cerebrum.

Discussion. A further visit to the farm established that the calf had probably collided with a protruding hinge whilst frisking in the yard.

Case 2

History. A 6-year-old Ayrshire cow (calved 2 months) was found in a field recumbent, unable to stand and in a comatosed state. Apparently the cow was normal during the morning and was found in the afternoon in this condition when the herd was brought up for evening milking.

Examination. The cow appeared unconscious with rumenal tympany. The pulse was slow, steady and regular.

The heart sounds were normal, and respiration was slow, deep and regular.

Diagnosis and Treatment. Although the symptoms were not quite typical it was taken to be a hypocalcaemia and 400 c.c. of calcium phosphate were given intravenously.

When examined that evening the cow was in the same state as when first seen. Rumenal tympany had increased and a cannula was inserted into the rumen. It was now apparent that this was not a metabolic disorder and a brain affection was suspected.

The following morning the animal was still in the same condition and slaughter was advised.

Post-mortem *Findings*

No skin damage around the head could be found. On the removal of skin from the frontal bones a depression 2½ in. × 3 in. just below the frontal eminence was seen. Haemorrhage into the cranial cavity had occurred.

Discussion. It is very difficult to understand how such an injury could have occurred to a cow grazing in a field. There were some men working on a pylon in the field and it is possible that she had approached them and had been struck by a heavy spanner.

Conclusion

Until these 2 cases had been seen we had not realised with what ease a fracture of the skull, with severe cerebral damage, could occur in an animal.

Immunity to Helminths.—*Concluded*

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LABORATORY ANIMALS CENTRE

A Symposium on the Provision of Animals for Cancer Research will be held at the Royal Society of Medicine, Wimpole Street, London, W.1, on Monday, May 23rd, 1960. The Chairman will be Professor J. S. Mitchell, Regius Professor of Physic, University of Cambridge, and the programme will include:—

"Fundamental programmes in causation, prevention and therapy," Professor Alex. Haddow.

"Spontaneous tumours in mice," Dr. P. R. Peacock.

"Present trends and future applications in the use of animals for research in carcinogenesis and tumour chemotherapy," Dr. D. L. Woodhouse.

"Some problems of cancer chemotherapy from the chemist's point of view," Professor F. Bergel.

"Laboratory animals and metastasising tumours," Dr. P. Loustalot.

"The epidemiology of polyoma virus in a mouse colony," Dr. M. H. Salaman and Dr. K. E. K. Rowson.

"Pitfalls in the production of cancer cells for experimental purposes," Dr. F. Kingsley Sanders.

This Symposium is open (without further invitation) to scientific, medical, and veterinary graduates, for whom it is primarily intended; senior animal technicians will also be welcome. Any enquiries about this Symposium should be addressed to the Director, Laboratory Animals Centre, M.R.C. Laboratories, Woodmansterne Road, Carshalton, Surrey (Telephone: Wallington 5512).

News and Comment

ADVISORY COMMITTEE ON SCIENTIFIC WORK OF INFESTATION CONTROL LABORATORY

The Minister of Agriculture, Fisheries and Food has appointed a Committee, under the chairmanship of Professor J. B. Cragg, B.SC., M.SC., Professor of Zoology in the University of Durham, " to advise and report annually on the programme of experimental and research work on infestation control, and on the co-ordination of that work with related work elsewhere." The Laboratory is part of the Advisory Service and Infestation Control Division and is situated at Tolworth, near Surbiton, with a field station at Worplesdon, near Guildford.

The members of the Committee are:—

Mr. H. R. Hewer, M.SC., Reader in Zoology, Imperial College of Science and Technology;

Dr. T. Moran, C.B.E., D.SC., PH.D., Director of Research for the Research Association of British Flour Millers, St. Albans, Herts;

Mr. F. Rayns, C.B.E., M.A., Director of the Norfolk Agricultural Station, Sprowston, Norwich;

Professor H. G. Sanders, M.A., PH.D., Chief Scientific Adviser (Agriculture), Ministry of Agriculture, Fisheries and Food;

Professor V. C. Wynne-Edwards, M.A., F.R.S.C., Department of Natural History, University of Aberdeen.

The Secretary of the Committee is Miss Y. Larthe, B.SC.

Assessors to the Committee are:—

Mr. A. S. Fortune, C.B.E., T.D., B.SC. (AGR.), Chief Inspector, Department of Agriculture for Scotland;

Dr. R. A. E. Galley, PH.D., A.R.C.S., D.I.C., F.R.I.C., Director, Tropical Products Institute, Department of Scientific and Industrial Research;

Mr. G. V. B. Herford, O.B.E., M.SC., Director, Pest Infestation Laboratory, Slough, Bucks;

Mr. G. G. Samuel, M.SC., Agricultural Research Council;

Dr. E. B. Worthington, M.A., PH.D., Deputy Director-General (Scientific), Nature Conservancy.

The Laboratory is the development and advisory centre for work on the control of insect infestation of stored products and is the centre for research and development work on the control of mammal and bird pests of agriculture. It acts as an instruction and liaison centre and runs courses for officers of overseas governments in the above matters. Its scientific and technical work falls into the following categories:—

(a) The discovery and control of insect infestations in all stored products and the development and application of chemical and other methods of control.

(b) Research into the biology and control of rats, mice, rabbits, moles, pigeons, and other mammals and birds injurious to agriculture and food.

RESEARCH STUDY GROUP ON TOXIC CHEMICALS IN AGRICULTURE

The Research Study Group, which was appointed by Ministers to study the need for further research into the effects of the use of toxic chemicals in agriculture and food storage, has begun its inquiries.

The Group is prepared to receive written evidence of views on the subject of the inquiry from persons or organisations. Written evidence should be addressed to the Secretary of the Group, Dr. E. J. Miller, Plant Pathology Laboratory, Hatching Green, Harpenden, Herts.

UNIVERSITY NEWS

Glasgow

Third professional examination for the degree of B.V.M.S., Part II

Veterinary Pathology, Bacteriology, and Parasitology

The following candidates have passed:—

Alexander, G. F.; Atarg, P.; Casserly, J. J.; Crawford, I.; Dabell, J. S.; Deans, R. W.; Ferguson, D. A.; Galbraith, B. D.; Heeley, Miss R. M.; Hodges, T. G. G.; Ingram, J. F. W.; Kenyon, Miss D. M.; Law, W. A.; Mackenzie, W. I.; Mclelland, J.; Macleoed, M.; Martin, E. C.; Miller, D. J. S.; Miller, T. A.; Mollison, A : Peek, I. S.; Richards, R. S.; Russell, T. M.; Saunders, R. W.; Selwan, I. E.; Shaw, D.; Smeaton, P. D.; Smith, G. A.; Todd, J. N.; Wilson, A. F. W.; Wilson, R. J. W.; Wisheirt, D. F.; Wyburn, R. S.; Young, I. M.; and Young, R. G. E.

MR. J. P. RAILTON

Mr. A. Lance Hughes writes:—

At a time when A. G. Street bemoans the uniformity and lack of characters in country life Mr. J. P. Railton could not fail to be prominent. His immaculate band-box figure was familiar for many years around the Welsh border counties, and few people figured in more anecdotes, told affectionately over many a farm fireside. For he had practised at Builth Wells and Kington before finally realising a lifelong ambition and settling in a lovely house in the beautiful village of Glasbury-on-Wye.

It often came as a surprise to those who knew his energy and attack in his practice, when they realised that " Joe " was a sincere home-lover, and once he had closed the gates of his drive he submerged in the tranquillity of a happy home life with his gracious wife and their son and daughter.

His forte was without doubt the examination of the horse for soundness and on this his opinion was sought for many miles. But he gave of his best whatever he undertook.

After the loss of his wife his life was an incredible battle against chronic illness but right to the end he had courage and to spare.

He will, perhaps, be remembered for much longer than those of us who are cast in a more orthodox mould.

R.C.V.S. OBITUARY

We record with regret the death of the following member of the profession:—

LITTLER, Samuel Barratt, of 243, Warwick Road, Kenilworth, Warwicks. Graduated Edinburgh, July 9th, 1936. Died Saturday, April 9th, 1960, aged 47 years.

PERSONAL

Mr. Eric I. Williams is leaving for the United States on May 4th to carry out a tour of study sponsored by a Wellcome Travel Research Grant. Mr. Williams will stay at Cornell University, Oklahoma State University, and Pennsylvania State University over a period of 5 weeks.

Births

MEADOWS.—On April 5th, 1960, at Avonside Hospital, Evesham, to Elsa (*née* Milburn, S.R.N., S.C.M.) and Graham Meadows, B.V.SC., M.R.C.V.S., a daughter, Jennifer Lindsay.

PHILLIPS.—On April 11th, 1960, at Groundslow Hospital, Stafford, to Diana, wife of D. H. Phillips, a daughter, Siwan Mafanwy Victoria.

WHITAKER.—On February 28th, 1960, to Cecilie, wife of D. Lloyd Whitaker, M.R.C.V.S., Farnborough House, Queens Road, Cheltenham, a daughter, Edwyna Catherine.

COMING EVENTS

April

27th (Wed.). Meeting of the Staffordshire and Derbyshire Veterinary Club at the White Hart, Uttoxeter, 7.30 p.m.

4th Annual General Meeting of the Metropolitan Region of the B.S.A.V.A., at the Royal Society of Medicine, Wimpole Street, London, W.1, 7.30 p.m.

29th (Fri.). Meeting of the Yorkshire Veterinary Society at the Royal Station Hotel, York, 2.30 p.m.

Extraordinary Meeting of the Essex Veterinary Society in the Conference Room of the Ministry of Agriculture, Beeches Road, Chelmsford, 2.30 p.m.

30th (Sat.). Meeting of the N.W. Region of the B.S.A.V.A. at the Queen's Hotel, Manchester, 7.30 p.m.

Dinner and Dance of the Central Veterinary Society at the Fellows Restaurant of the Zoological Society, Regent's Park, N.W.1, 7 p.m.

Annual General Meeting of State Veterinary Officers in the auditorium of the Wellcome Research Institute, 183-193 Euston Road, London, N.W.1., 4 p.m. The Annual Dinner will follow at the Criterion Restaurant at 6.30 p.m.

May

2nd (Mon.). Meeting of the East Yorkshire Clinical Club at the Talbot Hotel, Malton, 8 p.m.

4th (Wed.). Spring Meeting of the Eastern Counties Veterinary Society at Babraham Hall, Cambridge, 2.15 p.m.

Annual General Meeting of the South East Midlands Veterinary Association at the Grand Hotel, Northampton, 7.30 p.m.

Meeting of the Cornwall Veterinary Clinical Club at Gwendroe, Barrack Lane, Truro, 7.30 p.m.

5th (Thurs.). Annual General Meeting of the Central Veterinary Society at the Royal Veterinary College, Camden Town, N.W.1, 6 p.m.

6th (Fri.). Annual Dinner of R.V.C.A. at the Royal Veterinary College, Camden Town, N.W.1, 6.30 p.m.

Annual Dance of Midland Counties Veterinary Association at Eaton Lodge Hotel, Rugeley, 8 p.m. to 1 a.m.

11th (Wed.). Annual General Meeting of the B.S.A.V.A. Midland Area at the Queen's Hotel, Birmingham, 8 p.m.

12th (Thur.). Meeting of the South-Eastern Veterinary Association at the Royal Star Hotel, Maidstone, 7 p.m.

14th (Sat.). Annual Reunion and Dinner Dance of the Chiron Club at the Grand Atlantic Hotel, Weston-super-Mare, 7 p.m.

18th (Wed.). Meeting of the Lancashire Veterinary Association at Chester, 7.30 p.m.

June

10th (Fri.). Annual Dinner of the R.A.V.C. Officer's Club at the Naval and Military Club, 94, Piccadilly, London, W.1.

July

6th (Wed.). Meeting of the Technical Development Committee of the B.V.A., at 7, Mansfield Street, 10.30 a.m.

August 28th to September 3rd. 78th Annual Congress of the British Veterinary Association in Glasgow.

ADDRESSES OF DISEASE INFECTED PREMISES

The list given below indicates, first the county in which are situated the premises on which disease has been confirmed, followed by the postal address and date of outbreak.

Anthrax

Northumberland. West Hills Farm, Rothbury, Morpeth (Apr. 8).

Fowl Pest

Beds. Moor End, Eaton Bray, Dunstable (Apr. 8); The Piggery, Caves Lane, Bedford (Apr. 10); Dove House Farm, Wyboston (Apr. 12).

Essex. Roselawn, Broomfield, Chelmsford (Apr. 12); Smiths Green Farm, Debden, Saffron Walden (Apr. 13).

Hants. Salisbury Lane Farm, Middle Wallop, Stockbridge (Apr. 12).

Hunts. Caxton Road, Great Gransden; 41, London Street, Godmanchester, Huntingdon; Norfolk House Orchard, Earing Street, Godmanchester, Huntingdon; 2, King Willow Cottages, Hilton, St. Ives, Huntingdon; London Road Site, Fenstanton, Huntingdon (Apr. 9); 5, New Street, Godmanchester, Huntingdon (Apr. 11); Glebe Farm, Graveley; 1, Latin Close, Offord Cluny, Huntingdon; Wyboston Farm, Offord Road, Godmanchester, Huntingdon (Apr. 12); 19, Latin Close, Offord Cluny, Huntingdon (Apr. 13).

Kent. The Sceptre Hotel, Southborough, Tunbridge Wells (Apr. 13).

Lincs. North Road Farm, Great Ponton, Grantham (Apr. 11).

Northants. Hostel Farm, Sibson, Sibson-cum-Stibbington, Wansford, Peterborough (Apr. 8).

Notts. Rookswood Site, Bilsthorpe, Newark (Apr. 9); Haughton Farm, Haughton, Retford; Whitemoor Farm Cottage, Perlethorpe, Newark (Apr. 13).

Surrey. Glenside, Gadbridge Lane, Wehurst, Cranleigh; 9, Almners Road, Lyne, Chertsey (Apr. 8); Moat Cottage, Elstead, Godalming (Apr. 12).

Warwicks. Clapham Terrace Allotments, Leamington Spa (Apr. 8); Nonsuch Farm, Bartley Green, Birmingham, 32 (Apr. 10); Clapham Terrace Allotments, Leamington Spa (Apr. 11).

Worcs. Park Attwood Farm, Trimley, Bewdley (Apr. 12).

Letters to the Editor

The views expressed in letters addressed to the Editor represent the personal opinions of the writer only and their publication does not imply endorsement by the B.V.A.

SCIENTIFIC

A Serological Relationship Between Swine Fever and Mucosal Disease of Cattle

Sir,—The Ouchterlony technique (1948) of double diffusion in agar gel was first used to demonstrate a specific antigen-antibody reaction in swine fever by Molnar (1954a, 1954b). He was able to show that tissues containing swine fever virus, *i.e.* viraemic defibrinated blood, lymph node suspensions and crystal violet vaccines, produced a precipitin line when tested against swine fever antiserum. Mansi (1957) further reported that the pancreas was the optimum tissue which could be used to demonstrate antigen.

Experiments are in progress in this laboratory to investigate the value of a similar technique when applied to the diagnosis of mucosal disease in cattle. Tissues from cattle suspected of having the disease are used as antigen in tests against mucosal disease antisera. Starting with infective materials from field cases these antisera were originally prepared in cattle during the course of experiments by Huck (1957), employing one or more injections of viraemic blood which had been obtained after serial passage in calves.

In the course of the investigations using Ouchterlony plates, it was seen that lines between the homologous swine fever and mucosal disease systems in the same plate formed a continuous line of identity, suggesting a relationship between the two.

In gel diffusion analyses, the coincidence of precipitation lines, *i.e.* line of identity, between any two systems may or may not suggest a complete immunological identity; a lack of coincidence would indicate that a difference existed. The existence of a real serological relationship between the systems is supported by the following observations:—

1. No cross-reactions were obtained when either antigen was tested against antisera prepared against the viruses of canine distemper, canine hepatitis, myxomatosis, fibroma, swine pox, vaccinia, Newcastle disease, rinderpest*, Talfan, Teschen or against *Mycobacterium johnei*. Similarly, no reactions were obtained with the antisera tested against the tissue antigens of canine distemper, canine hepatitis, myxomatosis, fibroma, swine pox, Newcastle disease and vaccinia, or against a tissue culture Talfan virus and concentrated *M. johnei* antigen.

2. The cross-relationship was maintained in individual independent tests. Pancreases from 50 pigs experimentally infected with swine fever and 10 from healthy pigs were tested separately against swine fever and mucosal antisera. These yielded identical results. Likewise, with 454 bovine tissues from animals suspected of having died of mucosal disease, there was a 98 per cent. correlation between tests conducted with the respective antisera. Tissues from 20 clinically healthy slaughter-house cattle did not react with either antiserum.

3. The specific antibody in either system could be removed by absorption under suitable conditions with both the homologous and heterologous antigen. Thus, the capacity of swine fever tissue to remove mucosal disease antibody or mucosal disease tissue to remove swine fever antibody confirms a cross-relationship and indicates that a true antigen-antibody reaction is involved. Suitable controls, using normal tissues and sera, were incorporated throughout. The disappearance of the lines after absorption of the sera was not caused simply by dilution with tissue fluids.

4. The cross-reaction was obtained with a number of sera of both types and was not the property of any particular serum.

These experiments suggest a close serological relationship between the viruses of swine fever and those of the mucosal disease complex of cattle but interpretation of results must necessarily await further study. It may be postulated that the antigens detected are the viruses themselves, a soluble antigen or possibly a product of cells damaged by virus growth. The antisera used would then contain the antibodies to this common auto-antigen.

It is unlikely that the viruses of swine fever and mucosal disease are identical, but the possibility of their being related to each other immunologically, in the same way as rinderpest and distemper, is now being tested in both calves and pigs.

Yours faithfully,

J. H. DARBYSHIRE.

Central Veterinary Laboratory,
New Haw, Weybridge,
Surrey.
April 11th, 1960.

References

HUCK, R. A. (1957). *J. comp. Path. & Ther.* **67**. 267.
MANSI, W. (1957). *Ibid.*, **67**. 297.
MOLNAR, I. (1954a). *Acta. vet. hung.* **4**. 247.
———. (1954b). *Mag. Allatorv. Lapja.* **9**. 146.
OUCHTERLONY, O. (1948). *Ark. Kemi. Mineral, Geol.* **26B**. 1.

* Received from the Director, East African Veterinary Research Organisation, Muguga, Kenya.

A New Parasite of the Eland

Sir,—We would like to record the demonstration of a hitherto undescribed protozoan parasite of the eland (*Taurotragus oryx oryx* Pallas).

A young eland was found recumbent on the plains about 12 miles from Nairobi in Kenya. It did not resist capture and was transported in the back of a Land-Rover to a stable a few miles away. On arrival the animal was seen to pass urine of a port-wine colour and one of us was requested to treat it. The superficial lymph-nodes were enlarged, the temperature fluctuated around 103° F., and thin blood films showed a very heavy infection (over 90 per cent.) of the erythrocytes. Treatment consisted of a single dose of quinuronium sulphate and 2 daily doses of

oxytetracycline hydrochloride. Thin blood films and smears from the superficial lymph-nodes were prepared daily and ticks were collected and preserved. The eland remained tractable, ate green food, and drank water during the 3 days of treatment. The urine gradually became normal in colour but death occurred abruptly and unexpectedly on the evening of the third day of captivity. Autopsy revealed an icteric carcase.

Pieces of liver, lung, spleen, kidney, and lymph-nodes were collected and fixed in 10 per cent. formol saline; smears were also prepared from these tissues. The animal was heavily infested with ticks and many, including engorged nymphae, were collected. The engorged nymphae were allowed to moult to adults. The blood and tissue smears were fixed with methyl alcohol and stained with Geimsa. We were surprised that we were unable to demonstrate typical theilerial schizonts in the tissue smears since the blood films suggested that East Coast fever was the cause of death and both Lichtenheld (1911) and Beaumont (1939) had previously described apparent cases of E.C.F. in eland. A few schizonts, similar to those of *Theileria parva*, were seen, after a long search, in a smear of the liver.

Sections were stained with Haematoxylin and Eosin, Haematoxylin and Geimsa, and also by the Geimsa-colophonium method of Shortt and Cooper (1948). The latter method gave the best results. Parasites were not seen in sections of the spleen or kidney but sections of the liver, lymph-nodes, and lung showed many schizonts of the Cytauxzoon type. Dr. W. O. Neitz kindly examined these parasites and stated that they were indistinguishable from those he saw in a duiker (*Sylvicapra grimmia*) and in a kudu (*Strepsiceros strepsiceros strepsiceros*). These parasites have been described as *Cytauxzoon sylvicaprae* by Neitz and Thomas (1948) and *C. strepsicerosi* by Neitz and De Lange, 1956 (Neitz, 1957). We are also very grateful to Professor P. C. C. Garnham who examined sections and agreed that the parasite should be placed in the genus Cytauxzoon.

The schizonts were particularly numerous in the liver. In this organ they appeared in localised foci, often surrounding, or scattered within, an area of necrosis. We could not be certain of the host cell of all of the parasites, since some had obviously destroyed their host cells, but some small schizonts appeared to be within liver parenchyma cells. The larger masses often were within syncytial cells, some of which had as many as 35 nuclei. Cytomere formation was apparent in many of the larger schizonts but did not appear to be inevitable or necessary for the production of merozoites. Small merozoites could be seen on the periphery of some schizonts and also free in the liver sinusoids. Fifty schizonts were measured at random from one liver section and varied in size from $10 \times 10\ \mu$ to $175 \times 68\ \mu$, with an average of $58 \times 34\ \mu$.

In lung sections schizonts were generally smaller and always occurred within blood vessels, usually arterioles. In the lymph-nodes they again occurred in localised foci and were similar to the parasites in the liver.

The ticks collected from the eland included about 100 fully engorged nymphae of *Rhipicephalus appendiculatus*. After these had moulted to adults 10 of them were allowed to feed on a rabbit. They were removed from the rabbit on the 4th, 5th, 6th, and 7th days after attachment and were sectioned and stained by the Geimsa-colophonium method. Parasites were seen in one tick which was removed on the 5th day and in another which was removed on the 7th day. In both cases only one salivary gland cell was infected and the parasites were similar to the same stage of *T. parva* (Reichenow, 1940).

Although we cannot be certain that the eland was not infected with more than one parasite, it is very likely that all the forms mentioned above represent stages in the life cycle of one organism.

Since the tissue stages are indistinguishable from the parasites previously described as Cytauxzoon species, we provisionally name this parasite *C. taurotragi* sp. nov. We would like to suggest that further study of this organism may necessitate a redefinition of the genus or its removal to another sub-order.

A full description will be published later.

Yours faithfully,

HEATHER MARTIN.

Makerere College Veterinary School,
P.O. Kabete,
Kenya.

D. W. BROCKLESBY.

East African Veterinary Research Organisation,
Muguga,
P.O. Box 32,
Kikuyu,
Kenya.

March 31st, 1960.

References

BEAUMONT, E. (1939). *Vet. Rec.* **51**. 1311.
LICHTENHELD, G. (1911). *Z. Infekt. Haust.* **9**. 155.
NEITZ, W. O. (1957). *Onderstepoort J. vet. Sci.* **27**. 275.
———, & THOMAS, A. D. (1948). *Ibid.* **23**. 63.
REICHENOW, E. (1940). *Arch. Protistenk.* **94**. 1.
SHORTT, H. E., & COOPER, W. (1948). *Trans. roy. Soc. trop. Med. Hyg.* **41**. 427.

GENERAL

Superfoetation in the Bovine Animal

Sir,—Your readers may be interested in a case of superfoetation which occurred in a local A.I. member's herd. The subject was an aged Friesian type cow which had calved single calves normally in 5 successive years to A.I. In June, 1958, she was put to A.I. again and subsequently on 3 occasions at normal intervals after which she appeared to hold.

The owners presumed that she had held to the last service and were surprised when she was found one morning, 2 months before she was due, licking over a live, full-term heifer calf which was quite obviously hers. Her yield, however, was disappointing and she was left at grass to suckle the calf. Two months later she suddenly bagged up well and calved a live, full-term bull calf in circumstances that left no doubt that it was hers, also.

Several cases of superfoetation are on record through the Board's National Milk Recording organisation but the longest period so far shown

between deliveries is 36 days. To be sure of the parentage of the calves in this case blood samples from them, the cow, and the 4 different A.I. bulls used were sent to the Copenhagen blood type laboratory with the result that both calves were found to be out of the cow concerned, but only the second calf was by the bull stated. This led to more local enquiries and to the very strong probability that the first calf was by a neighbour's bull, service from which was presumably stolen at some time during the oestrus in which the first A.I. service was given.

A case is described by Dalrymple and Jenkins in the *Cornell Veterinarian* (1951) which occurred in a well-managed herd using natural service. The first foetus was a month premature and soon died, but was followed 3½ months later by a live, full-term calf. A German case describes the simultaneous birth of a live, full-term calf and a dead but recently living and normally formed 6-month foetus indicating conceptions 3 months apart. The remarkable features of the case we experienced were that an effective insemination did not disturb a 2-month foetus, nor did the pressures of a full-term calving on one side affect a 7-month embryo on the other. Both cleansings came away quickly and easily. Examination after a while showed the uterus to be quite normal and the ovaries small and anoestrous.

Yours faithfully,

E. J. SIMMONS,
Veterinary Officer.

Milk Marketing Board Cattle Breeding Centre,
Rivers Corner,
Sturminster Newton,
Dorset.

April 7th, 1960

References

DALRYMPLE, D. B. H., & JENKINS, D. (1951). *Cornell Vet.* **41**. 340.

SMITH, G. F. (1960). Private communication.

WEWER, M. (1952). *Deutsch Tierarztl. Wschr.* **59**. 101.

" Progress "

Sir,—If the letter of Mr. John E. Sheppard (*Vet. Rec.* **72**. 296) can be taken as indicating the views and reactions of even a minority of farm livestock owners in Britain it merits close study by every veterinarian.

My particular interest is in the paragraph dealing with the qualifications of college-trained herdsmen and women as it bears on a subject upon which I have commented previously.

Although Mr. Sheppard does not state whether the college training of the herdsmen and women had been at degree, diploma, or certificate level his assessment of its value seems rather unrealistic. Even in courses for the degree only approximately 270, or in some centres 400, days are allowed for the study of soils, crops, machinery, farm and estate management *and animals* following the initial year in pure science subjects. In diploma and certificate courses these times are reduced and the standards lowered. This training follows different lines from that undertaken by the nurse in human medicine, but for the purpose of efficiency in the administration of treatments to patients it compares badly.

It is rather disturbing to know that Mr. Sheppard's faith in the value of agricultural education is widely held even in official circles, probably because few people outside the group intimately concerned have given the problem other than passing attention.

Yours faithfully,

Hilton of Murtle, JOHN C. GRANT.
Bieldside, Aberdeen.
April 11th, 1960.

P.S.—Need I say that the terms of the Veterinary Surgeons' Act, 1948, are not unknown to me.

Sir,—Your correspondent of April 9th provides a concise answer to the problem he poses.

One can well understand his willingness to purchase drugs from his veterinary surgeon " at the same price " as from his chemist if he can at the same time obtain free expert advice, but why should he expect free advice from his veterinary surgeon any more than he would from his legal advisor.

It is precisely this reluctance on the part of the farmer to pay for expert veterinary advice that has forced some veterinary surgeons to make their drugs carry a proportion of the practice overheads.

My Society strongly advocates that drugs should be supplied at face price plus a reasonable dispensing fee—this obviously necessitates the farming community playing its part by a willingness to pay for professional advice.

This approach would ensure the best possible relationship between the veterinary surgeon and client and enable them to work together as a team in the spirit desired by your correspondent.

Yours faithfully,

F. V. JOHN,
President, Society of Practising Veterinary Surgeons.
Penybryn,
Llandilo,
Carms.
April 15th, 1960.

XUM

Sir,—It is always refreshing and frequently salutary to hear the views of the other party, and I read with considerable interest, and indeed some sympathy, the letter from Mr. John Sheppard.

I am surprised that he should find members of the profession pompous and unwilling to explain the handling of cases to the people concerned. As Mr. Sheppard implies, it is difficult to see how the veterinarian can expect co-operation from the farmer or his stock men unless he is prepared to take them along with him.

In view, however, of the efforts made by members of the profession in the matter of further education by lecturing at agricultural colleges, training courses, farmers' meetings, and Young Farmers' Clubs, etc., I feel that there can be no serious criticism on these lines.

There is, however, one point in this letter which needs some clarification. Mr. Sheppard states that if the farmer can obtain the same preparations from chemists or veterinary surgeons *at the same price* he will buy from the veterinarian as he can obtain expert advice on the preparation's use. Is the implication of this paragraph that the said "expert advice" should be given free, gratis, and for nothing? Were the farmer always prepared to pay a reasonable fee for advice given by the veterinarian, and refrained from accepting that gratuitously offered by the drug salesmen, foodstuffs representatives, and other unqualified persons, the actual sales and distribution of drugs would be a matter of rather less importance to all those concerned.

Yours faithfully,
L. GUY ANDERSON.

49, Cambridge Street,
Aylesbury,
Bucks.
April 12th, 1960.

B.S.A.V.A. Yorkshire Region

Sir,—We are hoping to encourage the formation of an active section of the British Small Animal Veterinary Association in the Yorkshire area and propose to have a meeting for a general discussion on this subject at the Hotel Metropole, Leeds, on Wednesday, April 27th, at 8 p.m. We would like all members of the profession interested in small animals who would like to attend meetings in Yorkshire to come along for a general discussion on how best to arrange these. The meeting will be quite informal and it is hoped to arrange for some clinical films to be shown.

Yours faithfully,
P. J. BOTTOMLEY,
R. S. KAY.

14, Ashfield,
Bradford, 7.
April 13th, 1960.

The Relationship Between Age of Semen and Fertility

Sir,—Following Mr. D. H. L. Madden's letter in THE VETERINARY RECORD (**72**. 273), we have examined our data in the way he suggested. In general his calculations are correct and we agree that the drop in non-return conception rate between 25 and 48 days is greater in deep-frozen and old semen than in fresh semen. The point at issue, however, is not the method which one chooses to express the length of the intervals between inseminations but the interpretation of the meaning of these intervals. The most difficult question is whether a 36- to 48-day interval represents a double oestrous cycle or embryonic death. There are two indications that returns at this time are more likely to represent double cycles than embryonic death.

(1) When service intervals in our material were plotted on a daily basis there was a distinct peak at 41 to 42 days. If the returns were due to embryonic death it is surprising that the peak of these returns coincided exactly with the length of two normal oestrous cycles.

(2) If old or deep-frozen semen were responsible for embryonic death one would expect a difference in the 25- to 35-day group which is generally considered to be associated with early embryonic death. Our figures show that there was not a greater number of returns in the 25- to 35-day group, or in the over-48-day group, in deep-frozen than in fresh semen.

For a final answer concerning the interpretation of service intervals of 36 to 48 days, it will undoubtedly be necessary to turn to experimental rather than survey methods.

Yours faithfully,
HUGH BOYD.

Dartington Hall Cattle Breeding Centre,
Totnes,
Devon.

HUGH C. B. REED.

Somerset Cattle Breeding Centre,
Ilminster,
Somerset.
April 13th, 1960.

Veterinary Education—an Anomaly

Sir,—I have just read Mr. D. G. Earnshaw's letter in THE VETERINARY RECORD of April 16th. I must agree wholeheartedly with the opinion expressed.

Unless I am much mistaken the invitation for applications for the post concerned was also printed in the *lay* press!

I have never been able to understand why it should be possible to imagine that on general lines a person with "medical" qualifications should be worthy of greater remuneration for teaching a veterinary subject than a person with "veterinary medical" qualifications. I think that if our profession would abandon a misguided sense of inferiority and realise that the addition of the one word "veterinary" gives an enhanced qualification the sooner our profession would receive the respect it deserves, a respect which is so feebly and futilely upheld by our own organisations.

What alarms me even more is the fact that there are members of the R.C.V.S. holding supervisory and advisory positions in the Universities who do not actively uphold the dignity of our profession in regard to relative scales of remuneration.

Yours faithfully,
MILLER WATSON.

11, Annfield Place,
Glasgow, E.1.
April 15th, 1960.